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one or both countries, and agreement to focus on prehospital treatment, six task forces formulated recommendations for a national structure of prehospital EM by family physicians, ambulance nurses, and hospital physicians. The outcome of the workshops had fundamental and strategic functions, such as the formulation of definitions, essential for effective communication between the various groups in both countries. Most of these definitions are still used, although their origins are blurred. While participants took part as individuals, not as formal representatives, they had senior key roles at ministries, insurances, medical and professional organizations, and scientific committees. The issue of EM was placed in several policy agendas and the recommendations could be recognized in initiatives taken by the Dutch societies for ambulance care and trauma surgery and the Ministry of Health in later years [4]. The structure and conclusions of the workshop may have contributed to develop EM in other European countries [5]. The working concept of joint, open-minded, content-driven, and nonpolitical meetings remain fruitful for the development of EM in each European country.

Also with regard to the more recent past, the editorial needs some additional information where the article deals with the academic development. The editorial suggests to say that the first professor in EM in the Netherlands was appointed in Rotterdam in 2011. This is not correct: the first formal appointment of an academic chair in EM took place at the VU university medical center (VUmc) in Amsterdam in February 2002. As result of a strategic vision of the Board of Directors of the VUmc, I was bestowed this challenging position as professor ordinarius at the Department of Anaesthesiology. I pioneered from scratch in this position until 2009. My academic tasks were aimed at research and education, however, without department funding. In the 7 years of the appointment and amongst many other initiatives, over 30 EM-related studies and 15 EM-related book chapters have been published; 14 books co-edited, two world conferences [6,7], and 12 postgraduate EM courses hosted. I was honored by regular invitations to speak at conferences, such as those organized by the European Society of Emergency Medicine and I am still participating in the editorial board of this and other journals. During the academic period, many EM-minded friends have been made but I felt no reason to actively advocate the, at that time rather fluid and muddled, development of EM in the Netherlands that was still not recognized as a formal medical specialty. At the same time, several emergency physicians and students with interest in EM have been supervised in their research, some of which has been published in this journal [8,9].

A future based on incomplete knowledge and reporting of the past is very fragile. I expect that these additional notes will provide a more complete picture and help us to understand that other factors have been connected. More facets of the history of EM in the Netherlands are worthwhile to be remembered.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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Antidotes for cyanide poisoning

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We read with interest the review and guideline by Anseeuw *et al*. [1] titled 'Cyanide poisoning by fire smoke inhalation: an European expert consensus'. The authors reviewed the current literature succinctly and identified gaps in knowledge. They also elegantly reviewed the diagnosis of cyanide poisoning, which can be difficult. We concur with several of the authors' recommendations that had not been clearly stated in other guidelines. In particular, we agree that sodium thiosulphate does not readily penetrate cells and its effectiveness is limited, despite older reviews that have reported that it should be used alone for cyanide toxicity. In addition, we conducted a comparative trial of sodium thiosulphate and hydroxocobalamin [2]. In this clinically relevant model of cyanide-induced hypotension, we showed that sodium thiosulphate is not effective alone and it had 100% mortality [2]. We also agree that although hydroxocobalamin has adverse effects, in sum, it is simpler to use, has less severe effects, has beneficial vasopressor effects and thus

may be the best drug to use for severe cyanide toxicity [3]. Finally, we agree that hydroxocobalamin is effective in cyanide-induced cardiac arrest, and that additional doses may be needed, as evidenced in our study, which showed that hydroxocobalamin is as effective as intravenous epinephrine for cyanide-induced cardiac arrest [4].

However, we disagree that sodium thiosulphate adds to the effectiveness of hydroxocobalamin. We especially disagree that it improves outcome for severe cyanide-induced toxicity. We compared hydroxocobalamin to hydroxocobalamin with sodium thiosulphate and did not find a difference on group comparisons of vital signs, cyanide levels, other laboratory values and mortality [2]. In addition, on the basis of previous animal and human studies, if the patient does not respond to the vasopressor or the antidotal effects of hydroxocobalamin, the patient is unlikely to benefit from sodium thiosulphate, a drug that may take up to 30 min to take effect and is poorly transported into the mitochondrial membrane [2,5].

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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Antidotes for cyanide poisoning

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We wish to thank Bebarta for drawing our attention to the position of sodium thiosulfate in the treatment of cyanide toxicity and giving us the opportunity to clarify our statements.

Although sodium thiosulfate is considered an ineffective antidote for acute cyanide toxicity because of poor intracellular penetration, slow onset of effect, a short half-life, and limited distribution volume, it is often used in conjunction with other rapid-acting antidotes. Its use as a single antidote for acute cyanide toxicity is no longer supported or indicated [1,2].

Because of its immediate diffusion into the different tissue compartments, intravenously administered hydroxocobalamin has a rapid onset of action. Sodium thiosulfate acts as a sulfur donor to detoxify cyanide to thiocyanate by the enzyme rhodanese, whereas hydroxocobalamin binds cyanide and forms the nontoxic cyanocobalamin, which is renally excreted. Therefore, theoretically, there is a synergistic action of sodium thiosulfate and hydroxocobalamin [1,2].

Hydroxocobalamin and sodium thiosulfate can be combined safely. The only limitation is that sodium thiosulfate and hydroxocobalamin may not be mixed in the same vial because this induces the formation of inefficient thiosulfatocobalamin [3].

Although there may be a theoretically synergistic action of sodium thiosulfate and hydroxocobalamin in cyanide toxicity, there is no evidence to support this at the moment, either in human data, or in animal data. Bebarta *et al.* [4] have shown that sodium thiosulfate added to hydroxocobalamin shows no benefit for cyanide-induced shock in a swine model. The limitations to this study are the duration of the study model (limited to 60 min after the start of cyanide infusion) and the hemodynamic parameters as end points, instead of long-term sequelae [1,2,4].

In our guidelines, we focus on the fast-acting hydrogen cyanide and advocate the use of hydroxocobalamin as a first-line antidote. This monotherapy of hydroxocobalamin should be effective for severe cyanide toxicity, provided it is administered in sufficiently high doses. For this reason, we propose a dose of 70 mg/kg hydroxocobalamin, to be repeated if persistent signs of toxicity exist. There is no evidence for administering doses of hydroxocobalamin higher than 150 mg/kg.

Given the theoretically synergistic action and given the experience in the treatment of the toxicity of cyanide salts (or other forms of longer-acting cyanide toxicity), we propose the addition of sodium thiosulfate if lactate levels remain elevated or if other signs of cyanide toxicity persist despite administering the maximum dose of 150 mg/kg hydroxocobalamin. As clearly marked in the algorithm, sodium thiosulfate is considered as an adjuvant and a second-line antidote, and is administered after other treatments have been initiated.